

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-75 (Canceled)

76. (New) A composition, comprising:

- a metal;
- a chelator capable of chelating the metal;
- an indazole nonpeptide targeting moiety covalently bound to the chelator, either directly or via an optional interposed linking group, wherein the targeting moiety binds to a receptor that is upregulated during angiogenesis; and
- at least one of a chemotherapeutic agent or a radiosensitizer agent.

77. (New) The composition of claim 76, wherein the metal, targeting moiety, chelator, and optional linking group are a diagnostic or therapeutic metallopharmaceutical.

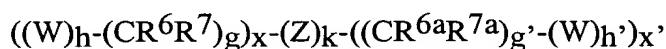
78. (New) The composition of claim 76, wherein the chemotherapeutic agent is mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, or leutinizing hormone releasing factor.

79. (New) The composition of claim 76, wherein the radiosensitizer agent is 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-

morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, or 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

80. (New) The composition of claim 76, wherein the linking group is present between the targeting moiety and the chelator.

81. (New) The composition of claim 76, wherein the linking group has a formula:



wherein:

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)NR⁸, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, (OCH₂CH₂)₂₀₋₂₀₀, (CH₂CH₂O)₂₀₋₂₀₀, (OCH₂CH₂CH₂)₂₀₋₂₀₀, (CH₂CH₂CH₂O)₂₀₋₂₀₀, and (aa)_t;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, and R⁸ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁₋₅ alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to the chelator;

R¹⁰ is independently selected at each occurrence from the group: a bond to the chelator, COOR¹¹, C(=O)NHR¹¹, NHC(=O)R¹¹, OH, NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy

substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R¹², aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², and a bond to the chelator;

R¹² is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5; and

x' is selected from 0, 1, 2, 3, 4, and 5.

82. (New) The composition of claim 76, wherein the receptor is $\alpha_v\beta_3$ or $\alpha_v\beta_5$.

83. (New) The composition of claim 76, wherein the metal is ^{99m}Tc, ⁹⁵Tc, ¹¹¹In, ⁶²Cu, ⁶⁴Cu, ⁶⁷Ga, or ⁶⁸Ga.

84. (New) The composition of claim 76, wherein the metal is ^{99m}Tc or ⁹⁵Tc.

85. (New) The composition of claim 76, wherein the metal is ^{99m}Tc.

86. (New) The composition of claim 76, wherein the metal is ¹¹¹In.

87. (New) The composition of claim 76, further comprising a first ancillary ligand and a second ancillary ligand.

88. (New) The composition of claim 77, wherein the metallopharmaceutical is:

^{99m}Tc (((4-(4-(((3-(2-(2-(3-((6-(diazenido)(3-pyridyl))carbonylamino)propoxy)ethoxy)ethoxy)propyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)amino)-3-((1-(3-(imidazole-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid) (tricine)(TPPTS);

^{99m}Tc (2-(2-((5-(N-(1,3-bis(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)ethyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)amino)propoxy)ethoxy)ethoxy)propyl)carbamoyl)propyl)carbamoyl)(2-pyridyl))2-diazenido) (tricine)(TPPTS);

^{99m}Tc (2-((6-(diazenido)(3-pyridyl))carbonylamino)-4-(N-(3-(2-(2-(3-(((4-(4-(((1-carboxy-2-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)ethyl)amino)sulfonyl)phenyl)phenyl)sulfonyl)amino)propoxy)ethoxy)ethoxy)propyl)carbamoyl)butanoic acid) (tricine)(TPPTS);

^{99m}Tc (2-(6-((6-(diazenido)(3-pyridyl))carbonylamino)hexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)-propanoic acid) (tricine)(TPPTS);

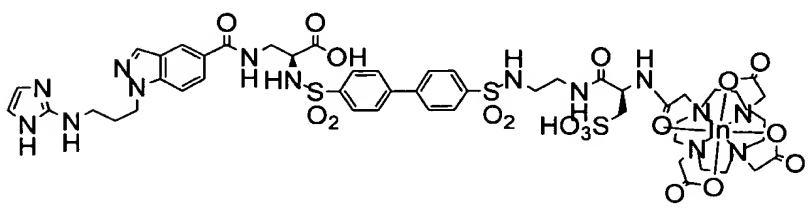
^{99m}Tc (2-((6-(diazenido)(3-pyridyl))carbonylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonylamino)propanoic acid (tricine)(TPPTS);

^{99m}Tc [2-[[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)) (tricine)(TPPTS); or

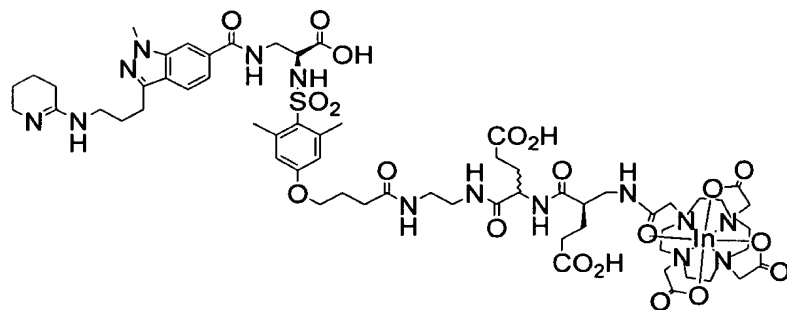
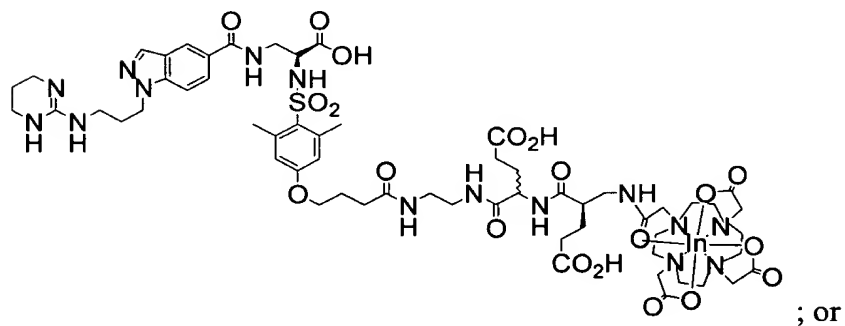
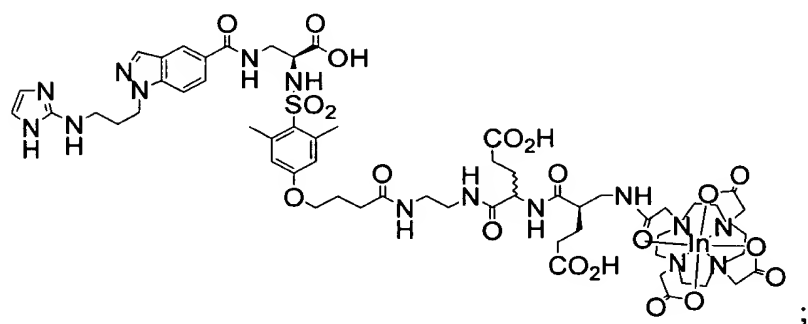
^{99m}Tc ([2-[[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu-bis-[Glu(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)(2-(6-aminohexanoylamino)-3-((1-(3-(imidazol-2-ylamino)propyl)(1H-indazol-5-yl))carbonyl-amino)propanoic acid)]] (tricine)(TPPTS).

89. (New) The composition of claim 77, wherein the metallopharmaceutical is:

PATENT



Office Action Dated: September 14, 2004

CC1=CC=C(C=C1)C(=O)NCC(NC(=O)O)S(=O)(=O)c2cc(C)c(OC(=O)NCCNC(=O)CC(C(=O)O)NCC(=O)N[C@@H]3C[C@H]4[C@@H](C[C@H]3C[C@H]4O)O)c(C)c2

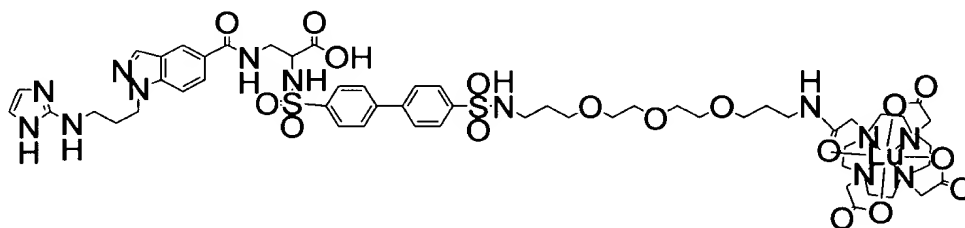
90. (New) The composition of claim 76, wherein the metal is ^{33}P , ^{125}I , ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , ^{109}Pd , ^{159}Gd , ^{140}La , ^{198}Au , ^{199}Au , ^{169}Yb , ^{175}Yb , ^{165}Dy , ^{166}Dy , ^{67}Cu , ^{105}Rh , ^{111}Ag , or ^{192}Ir .

91. (New) The composition of claim 76, wherein the metal is ^{153}Sm .

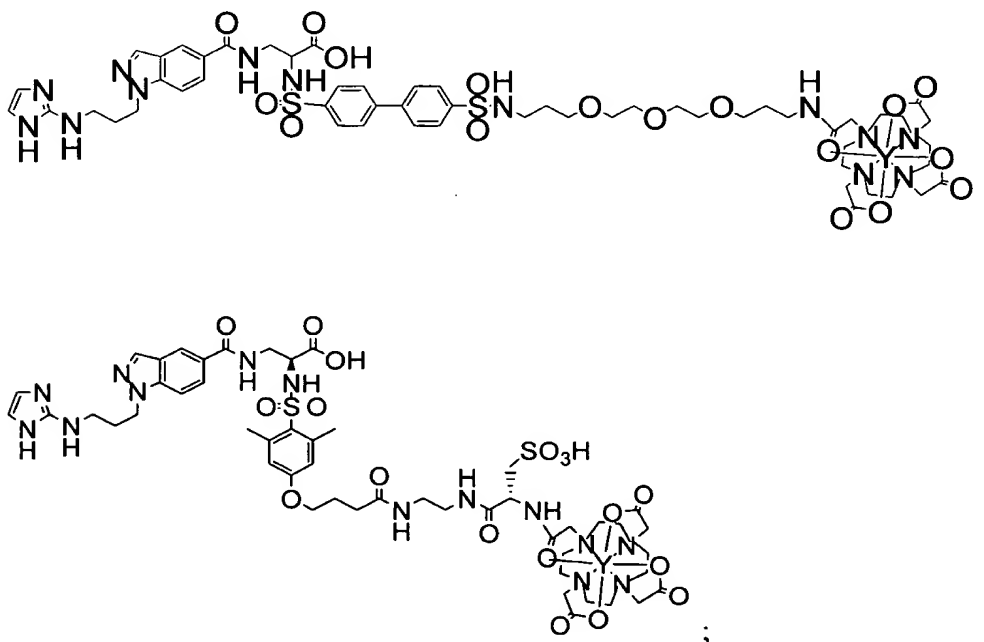
92. (New) The composition of claim 76, wherein the metal is ^{177}Lu .

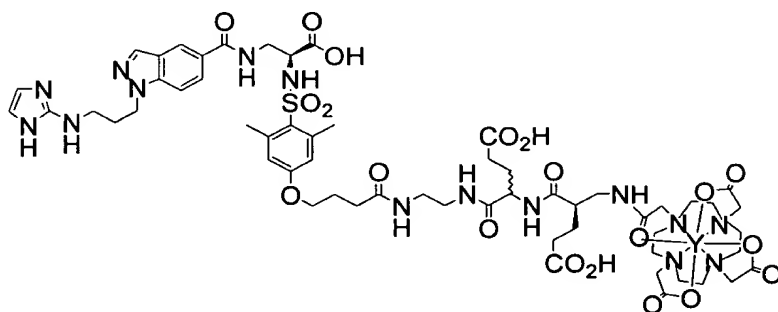
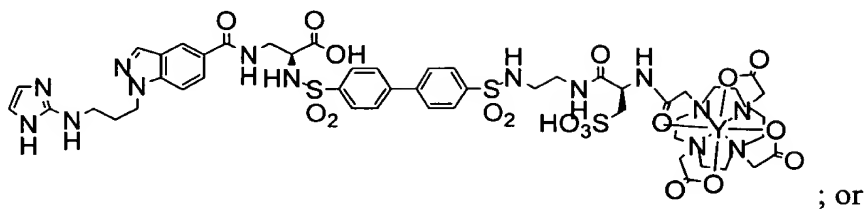
93. (New) The composition of claim 76, wherein the metal is ^{90}Y .

94. (New) The composition of claim 77, wherein the metallopharmaceutical is:



95. (New) The composition of claim 77, wherein the metallopharmaceutical is:



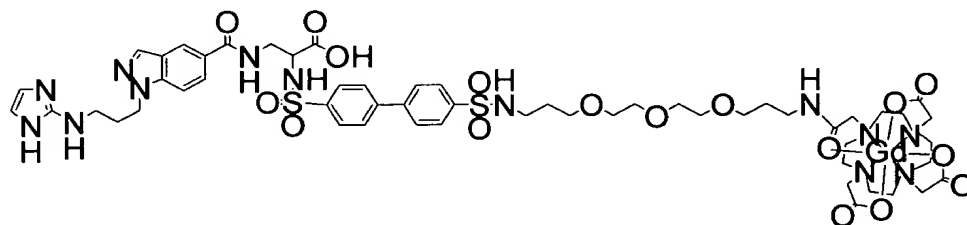


96. (New) The composition of claim 77, wherein the metallopharmaceutical is a MRI contrast agent, the metal is a paramagnetic metal ion selected from the group: Gd(III), Dy(III), Fe(III), and Mn(II), and the linking group is present between the targeting moiety and chelator.

97. (New) The composition of claim 96, wherein the receptor is $\alpha_v\beta_3$ or $\alpha_v\beta_5$.

98. (New) The composition of claim 96, wherein the metal ion is Gd(III).

99. (New) The composition of claim 77, wherein the metallopharmaceutical is:



100. (New) The composition of claim 77, wherein the metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, the receptor is $\alpha_v\beta_3$ or $\alpha_v\beta_5$, and the linking group is present between the targeting moiety and chelator.

101. (New) A composition, comprising:

an indazole nonpeptide targeting moiety attached to a surfactant via a linking group, wherein the targeting moiety binds to a receptor that is upregulated during angiogenesis; and an echogenic gas.

102. (New) The composition of claim 101, wherein the receptor is $\alpha_v\beta_3$ or $\alpha_v\beta_5$.

103. (New) The composition of claim 102, wherein the surfactant is a lipid or a compound

of the formula: $A^9-E^1-A^{10}$; wherein

A^9 is selected from the group: OH and OR^{27} ;

A^{10} is OR^{27} ;

R^{27} is $C(=O)C_{1-20}$ alkyl;

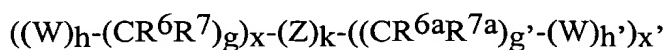
E^1 is C_{1-10} alkylene substituted with 1-3 R^{28} ;

R^{28} is independently selected at each occurrence from the group: R^{30} , $-PO_3H-R^{30}$, $=O$, $-CO_2R^{29}$, $-C(=O)R^{29}$, $-C(=O)N(R^{29})_2$, $-CH_2OR^{29}$, $-OR^{29}$, $-N(R^{29})_2$, C_1-C_5 alkyl, and C_2-C_4 alkenyl;

R^{29} is independently selected at each occurrence from the group: R^{30} , H, C_1-C_6 alkyl, phenyl, benzyl, and trifluoromethyl;

R^{30} is a bond to the linking group.

104. (New) The composition of claim 103, wherein the linking group has a formula:



wherein:

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR⁸C(=O), C(=O)NR⁸, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, (OCH₂CH₂)₂₀₋₂₀₀, (CH₂CH₂O)₂₀₋₂₀₀, (OCH₂CH₂CH₂)₂₀₋₂₀₀, (CH₂CH₂CH₂O)₂₀₋₂₀₀, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁰, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁰, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁰;

R⁶, R^{6a}, R⁷, R^{7a}, and R⁸ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁰, aryl substituted with 0-3 R¹⁰, benzyl substituted with 0-3 R¹⁰, and C₁₋₅ alkoxy substituted with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to S_f;

R¹⁰ is independently selected at each occurrence from the group: a bond to S_f, COOR¹¹, C(=O)NHR¹¹, NHC(=O)R¹¹, OH, NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R¹², aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², and a bond to S_f;

R¹² is a bond to S_f;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

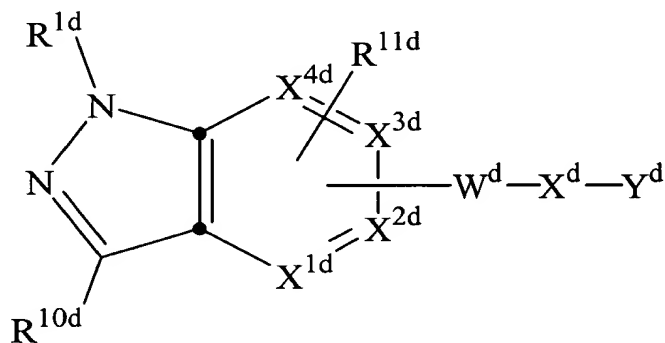
h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;
x is selected from 0, 1, 2, 3, 4, and 5; and
x' is selected from 0, 1, 2, 3, 4, and 5.

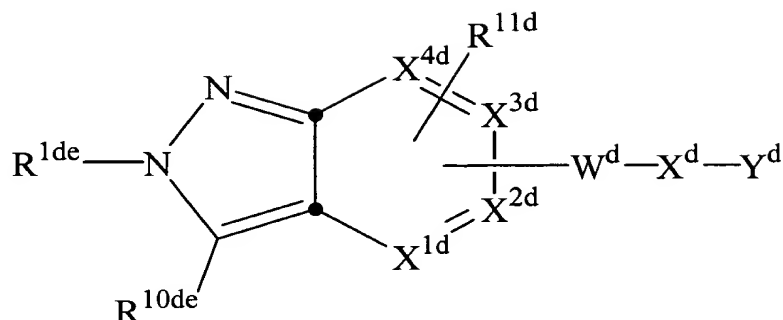
105. (New) The composition of claim 104, further comprising: 1,2-dipalmitoyl-sn-glycero-3-phosphatidic acid, 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine, and N-(methoxypolyethylene glycol 5000 carbamoyl)-1,2-dipalmitoyl-sn-glycero-3-phosphatidylethanolamine.

106. (New) The composition of claim 105, wherein the echogenic gas is a C₂₋₅ perfluorocarbon.

107. (New) The composition of 76 or 101, wherein the indazole nonpeptide is a compound of Formulae (Ia) or (Ib):



(Ia)



(1b)

including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof, wherein:

X^{1d} is CH, C- W^d - X^d - Y^d , or C bonded to the linking group;

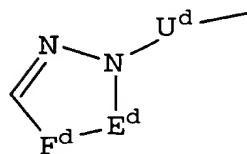
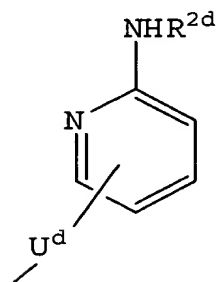
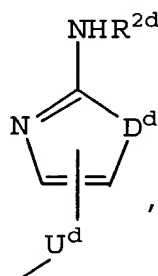
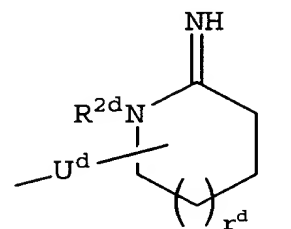
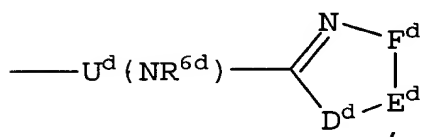
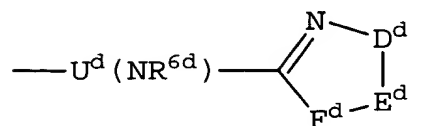
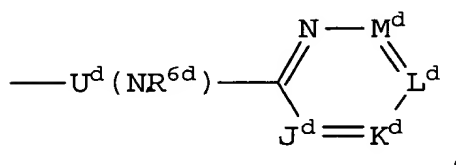
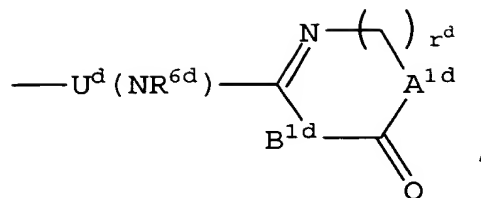
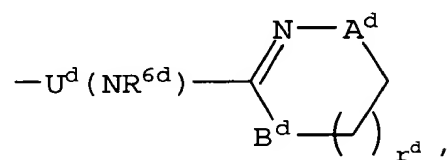
X^{2d} is CH or C- W^d - X^d - Y^d ;

X^{3d} is CR^{11d} or C- W^d - X^d - Y^d ;

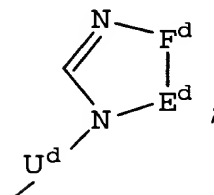
X^{4d} is CR^{11d} ;

R^{1d} is selected from: R^{1de} , C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{1de} is selected from:



or



A^d and B^d are independently $-\text{CH}_2-$, $-\text{O}-$, $-\text{N}(\text{R}^{2d})-$, or $-\text{C}(=\text{O})-$;

A^{1d} and B^{1d} are independently -CH₂- or -N(R^{3d})-;

D^d is -N(R^{2d})-, -O-, -S-, -C(=O)- or -SO₂-;

E^d-F^d is -C(R^{4d})=C(R^{5d})-, -N=C(R^{4d})-, -C(R^{4d})=N-, or -C(R^{4d})₂C(R^{5d})₂-;

J^d, K^d, L^d and M^d are independently selected from:

-C(R^{4d})-, -C(R^{5d})- and -N-, provided that at least one of J^d, K^d, L^d and M^d is not -N-;

provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is C- W^d- X^d- Y^d, and when R^{10d} is R^{1de} then X^{3d} is C- W^d- X^d- Y^d;

R^{2d} is selected from: H, C₁-C₆ alkyl, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl; (C₁-C₆ alkyl)aminocarbonyl, C₃-C₆ alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, heteroaryl(C₁-C₆ alkyl)carbonyl, heteroarylcarbonyl, aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl-, arylcarbonyl, C₁-C₆ alkylsulfonyl, arylsulfonyl, aryl(C₁-C₆ alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C₁-C₆ alkyl)sulfonyl, aryloxy carbonyl, and aryl(C₁-C₆ alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, CF₃, and nitro;

R^{3d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and heteroaryl(C₁-C₆ alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C₁-C₄ alkoxy, NR^{2d}R^{3d}, halogen, NO₂, CN, CF₃, C₁-C₆ alkyl, C₃-C₆ alkenyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, (C₁-C₆ alkyl)carbonyl, (C₁-C₆ alkoxy)carbonyl, arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, amino, CF₃, and NO₂;

U^d is selected from:

-(CH₂)_n^d-,

$-(CH_2)_n^d(CR^{7d}=CR^{8d})(CH_2)_m^d-$,
 $-(CH_2)_n^d(C\equiv C)(CH_2)_m^d-$,
 $-(CH_2)_t^dJ^d(CH_2)_m^d-$,
 $-(CH_2)_n^dO(CH_2)_m^d-$,
 $-(CH_2)_n^dN(R^{6d})(CH_2)_m^d-$,
 $-(CH_2)_n^dC(=O)(CH_2)_m^d-$,
 $-(CH_2)_n^d(C=O)N(R^{6d})(CH_2)_m^d-$,
 $-(CH_2)_n^dN(R^{6d})(C=O)(CH_2)_m^d-$, and
 $-(CH_2)_n^dS(O)_p^d(CH_2)_m^d-$;

wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d} ;

J^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

R^{6d} is selected from: H, C_1 - C_4 alkyl, or benzyl;

R^{7d} and R^{8d} are independently selected from: H, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, and heteroaryl(C_0 - C_6 alkyl)-;

R^{10d} is selected from: H, R^{1de} , C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN , CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{10de} is selected from: H, C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN , CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, -

SO₂NR^{17d}R^{20d}, C₁-C₆ alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₆ alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₃-C₇ cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, C₄-C₁₁ cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d}, aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d}, and aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d},

R^{11d} is selected from H, halogen, CF₃, CN, NO₂, hydroxy, NR^{2d}R^{3d}, C₁-C₄ alkyl substituted with 0-1 R^{21d}, C₁-C₄ alkoxy substituted with 0-1 R^{21d}, aryl substituted with 0-1 R^{21d}, aryl(C₁-C₆ alkyl)- substituted with 0-1 R^{21d}, (C₁-C₄ alkoxy)carbonyl substituted with 0-1 R^{21d}, (C₁-C₄ alkyl)carbonyl substituted with 0-1 R^{21d}, C₁-C₄ alkylsulfonyl substituted with 0-1 R^{21d}, and C₁-C₄ alkylaminosulfonyl substituted with 0-1 R^{21d},

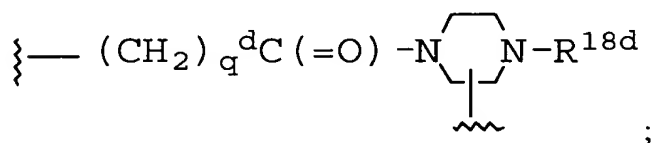
W^d is selected from:

-(C(R^{12d})₂)_q^dC(=O)N(R^{13d})-, and

-C(=O)-N(R^{13d})-(C(R^{12d})₂)_q^d;

X^d is -C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-; or

alternatively, W^d and X^d can be taken together to be



R^{12d} is selected from H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, and aryl(C₁-C₆ alkyl)-;

R^{13d} is selected from H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl, and aryl(C₁-C₆ alkyl)-;

R^{14d} is selected from:

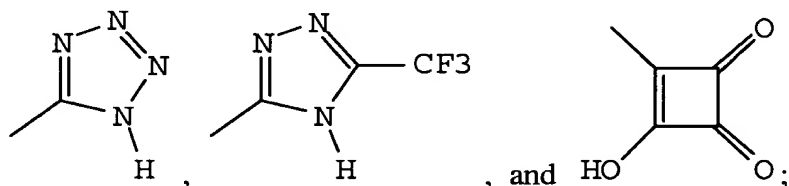
H, C₁-C₆ alkylthio(C₁-C₆ alkyl)-, aryl(C₁-C₁₀ alkylthioalkyl)-, aryl(C₁-C₁₀ alkoxyalkyl)-, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₆ hydroxyalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, and CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d},

R^{15d} is selected from:

H, R^{16d}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₁₀ alkylaminoalkyl, di(C₁-C₁₀ alkyl)aminoalkyl, (C₁-C₁₀ alkyl)carbonyl, aryl(C₁-C₆ alkyl)carbonyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, SO₂R^{17d}, and SO₂NR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R^{11d},

Y^d is selected from:

-COR^{19d}, -SO₃H, -PO₃H, tetrazolyl, -CONHNHSO₂CF₃, -CONHSO₂R^{17d}, -CONHSO₂NHR^{17d}, -NHCOCF₃, -NHCONHSO₂R^{17d}, -NHSO₂R^{17d}, -OPO₃H₂, -OSO₃H, -PO₃H₂, -SO₃H, -SO₂NHCOR^{17d}, -SO₂NHCO₂R^{17d},



R^{16d} is selected from:

-N(R^{20d})-C(=O)-O-R^{17d},
 -N(R^{20d})-C(=O)-R^{17d},
 -N(R^{20d})-C(=O)-NH-R^{17d},

$-\text{N}(\text{R}^{20\text{d}})\text{SO}_2-\text{R}^{17\text{d}}$, and

$-\text{N}(\text{R}^{20\text{d}})\text{SO}_2-\text{NR}^{20\text{d}}\text{R}^{17\text{d}}$;

$\text{R}^{17\text{d}}$ is selected from:

$\text{C}_1\text{-C}_{10}$ alkyl optionally substituted with a bond to the linking group, $\text{C}_3\text{-C}_{11}$ cycloalkyl optionally substituted with a bond to the linking group, aryl($\text{C}_1\text{-C}_6$ alkyl)- optionally substituted with a bond to the linking group, ($\text{C}_1\text{-C}_6$ alkyl)aryl optionally substituted with a bond to the linking group, heteroaryl($\text{C}_1\text{-C}_6$ alkyl)- optionally substituted with a bond to the linking group, ($\text{C}_1\text{-C}_6$ alkyl)heteroaryl optionally substituted with a bond to the linking group, biaryl($\text{C}_1\text{-C}_6$ alkyl)- optionally substituted with a bond to the linking group, heteroaryl optionally substituted with a bond to the linking group, aryl optionally substituted with a bond to the linking group, biaryl optionally substituted with a bond to the linking group, and a bond to the linking group, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group: $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkoxy, aryl, heteroaryl, halo, cyano, amino, CF_3 , and NO_2 ;

$\text{R}^{18\text{d}}$ is selected from:

$-\text{H}$,

$-\text{C}(=\text{O})-\text{O}-\text{R}^{17\text{d}}$,

$-\text{C}(=\text{O})-\text{R}^{17\text{d}}$,

$-\text{C}(=\text{O})-\text{NH}-\text{R}^{17\text{d}}$,

$-\text{SO}_2-\text{R}^{17\text{d}}$, and

$-\text{SO}_2-\text{NR}^{20\text{d}}\text{R}^{17\text{d}}$;

$\text{R}^{19\text{d}}$ is selected from: hydroxy, $\text{C}_1\text{-C}_{10}$ alkyloxy, $\text{C}_3\text{-C}_{11}$ cycloalkyloxy, aryloxy, aryl($\text{C}_1\text{-C}_6$ alkoxy)-, $\text{C}_3\text{-C}_{10}$ alkylcarbonyloxyalkyloxy, $\text{C}_3\text{-C}_{10}$ alkoxy carbonyloxyalkyloxy, $\text{C}_2\text{-C}_{10}$ alkoxy carbonylalkyloxy, $\text{C}_5\text{-C}_{10}$ cycloalkylcarbonyloxyalkyloxy, $\text{C}_5\text{-C}_{10}$ cycloalkoxy carbonyloxyalkyloxy, $\text{C}_5\text{-C}_{10}$ cycloalkoxy carbonylalkyloxy, $\text{C}_7\text{-C}_{11}$ aryloxy carbonylalkyloxy, $\text{C}_8\text{-C}_{12}$ aryloxy carbonyloxyalkyloxy, $\text{C}_8\text{-C}_{12}$ arylcarbonyloxyalkyloxy, $\text{C}_5\text{-C}_{10}$

alkoxyalkylcarbonyloxyalkyloxy, C₅-C₁₀ (5-alkyl-1,3-dioxo-cyclopenten-2-one-yl)methyloxy, C₁₀-C₁₄ (5-aryl-1,3-dioxo-cyclopenten-2-one-yl)methyloxy, and

(R^{1d})(R^{2d})N-(C₁-C₁₀ alkoxy)-;

R^{20d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and heteroaryl(C₁-C₆ alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}₂;

m^d is 0-4;

n^d is 0-4;

t^d is 0-4;

p^d is 0-2;

q^d is 0-2; and

r^d is 0-2;

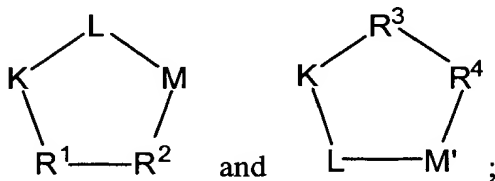
with the following provisos:

(1) t^d, n^d, m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and

(2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is

-(CH₂)_t^d J^d (CH₂)_m^d -; or

Q is a peptide selected from the group:



R¹ is L-valine, D-valine or L-lysine optionally substituted on the ε amino group with a bond to the linking group;

R² is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to the linking group;

R³ is D-valine;

R⁴ is D-tyrosine substituted on the hydroxy group with a bond to the linking group;

provided that one of R¹ and R² in each Q is substituted with a bond to the linking group, and further provided that when R² is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

108. (New) A therapeutic composition, comprising:

the composition of claim 76 and a parenterally acceptable carrier.

109. (New) A diagnostic composition, comprising:

the composition of claim 76 and a parenterally acceptable carrier.

110. (New) An ultrasound contrast agent composition, comprising:

composition of claim 101 and a parenterally acceptable carrier.